

Translation

PATENT COOPERATION TREATY

PCT

531,099

PCT/JP2003/012986



INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

| | | |
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| Applicant's or agent's file reference 1511 | FOR FURTHER ACTION See Form PCT/IPEA/416 | |
| International application No. PCT/JP2003/012986 | International filing date (day/month/year) 09 October 2003 (09.10.2003) | Priority date (day/month/year) 09 October 2002 (09.10.2002) |
| International Patent Classification (IPC) or national classification and IPC A61K 45/06, 31/567, A61P 35/00, 43/00 | | |
| Applicant KYOWA HAKKO KOGYO CO., LTD. | | |

- This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
- This REPORT consists of a total of 7 sheets, including this cover sheet.
- This report is also accompanied by ANNEXES, comprising:
 - ☐ (sent to the applicant and to the International Bureau) a total of _____ sheets, as follows:
 - ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
 - ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
 - ☐ (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) _____, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).
- This report contains indications relating to the following items:
 - ☒ Box No. I Basis of the report
 - ☐ Box No. II Priority
 - ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
 - ☐ Box No. IV Lack of unity of invention
 - ☒ Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
 - ☐ Box No. VI Certain documents cited
 - ☐ Box No. VII Certain defects in the international application
 - ☐ Box No. VIII Certain observations on the international application

| | |
|--|---|
| Date of submission of the demand 07 May 2004 (07.05.2004) | Date of completion of this report 28 September 2004 (28.09.2004) |
| Name and mailing address of the IPEA/JP | Authorized officer |
| Facsimile No. | Telephone No. |

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International Application No.

PCT/JP2003/012986

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

- ☐ This report is based on translations from the original language into the following language _____, which is language of a translation furnished for the purpose of:
- ☐ international search (under Rules 12.3 and 23.1(b))
 - ☐ publication of the international application (under Rule 12.4)
 - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

- ☒ The international application as originally filed/furnished
- ☐ the description:
- pages _____, as originally filed/furnished
- pages* _____ received by this Authority on _____
- pages* _____ received by this Authority on _____
- ☐ the claims:
- pages _____, as originally filed/furnished
- pages* _____, as amended (together with any statement) under Article 19
- pages* _____ received by this Authority on _____
- pages* _____ received by this Authority on _____
- ☐ the drawings:
- pages _____, as originally filed/furnished
- pages* _____ received by this Authority on _____
- pages* _____ received by this Authority on _____
- ☐ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages _____
- ☐ the claims, Nos. _____
- ☐ the drawings, sheets/figs _____
- ☐ the sequence listing (*specify*): _____
- ☐ any table(s) related to sequence listing (*specify*): _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

- ☐ the description, pages _____
- ☐ the claims, Nos. _____
- ☐ the drawings, sheets/figs _____
- ☐ the sequence listing (*specify*): _____
- ☐ any table(s) related to sequence listing (*specify*): _____

* If item 4 applies, some or all of those sheets may be marked "superseded."

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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 2, 8, 14, 20, 26, 32

because:

☒ the said international application, or the said claims Nos. 2, 8, 14, 20, 26, 32 relate to the following subject matter which does not require an international preliminary examination (*specify*):

See supplemental sheet

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. _____ are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 2, 8, 14, 20, 26, 32

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form

☐ has not been furnished

☐ does not comply with the standard

the computer readable form

☐ has not been furnished

☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

☐ see Supplemental Box for further details.

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Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: III. 1.

Claims 2, 8, 14, 20, 26 and 32 pertain to methods for treatment of the human body by surgery or therapy, and thus relate to subject matter which does not require international preliminary examination by this International Preliminary Examining Authority.

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V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

| | | | |
|-------------------------------|--------|---|-----|
| Novelty (N) | Claims | 1, 4-7, 10-13, 16-19, 22-25, 28-31, 34-36 | YES |
| | Claims | 3, 9, 15, 21, 27, 33 | NO |
| Inventive step (IS) | Claims | | YES |
| | Claims | 1, 3-7, 9-13, 15-19, 21-25, 27-31, 33-36 | NO |
| Industrial applicability (IA) | Claims | 1, 3-7, 9-13, 15-19, 21-25, 27-31, 33-36 | YES |
| | Claims | | NO |

2. Citations and explanations

Documents

1. WO 00/43408 A2 (Duquesne University of the Holy Ghost), 27 July 2000
2. WO 02/43704 (Kyowa Hakko Kogyo Co., Ltd.), 6 June 2002
3. WO 99/33858 A2, (SRI International), 8 July 2002
4. WO 01/81364 A1, (SRI International), 1 November 2001
5. Steroids, 1998, Vol. 63, No. 7/8, pp. 425-432
6. WO 02/64142 A1 (Janssen Pharmaceutica NV), 22 August 2002

Explanations

Claims 3, 9, 15, 21, 27 and 33

The inventions set forth in claims 3, 9, 15, 21, 27 and 33 are not novel and do not involve an inventive step in the light of documents 1-5, cited in the international search report.

Documents 1-5 disclose steroid sulphatase inhibitors comprising compounds represented by formula (I) in claim 7, formula (IA) in claim 13 or formula (IB) in claim 19; and given that these are specified in claim 3 as "for

concomitant use, at the same time or separated by a time interval, with a hormonal therapy agent and/or a chemotherapy agent", the steroid sulphatase inhibitors set forth in the aforementioned claims are indistinguishable from the steroid sulphatase inhibitors disclosed in documents 1-5, and the inventions set forth in the above claims are thus disclosed in documents 1-5.

A person skilled in the art could also suitably alter substituent groups in the compounds disclosed in documents 1-5, and attempt to confirm a steroid sulphatase inhibiting action as a result.

Claims 1, 4-7, 10-13, 16-19, 22-25, 28-31 and 34-36

The inventions set forth in claims 1, 4-7, 10-13, 16-19, 22-25, 28-31 and 34-36 are not disclosed in any of the documents cited in the international search report, and are novel; however, they do not involve an inventive step in the light of documents 1-6

Documents 1-5 claim that compounds represented by formula (I) in claim 7, formula (IA) in claim 13 or formula (IB) in claim 19 are useful for treating cancers dependent on hormones such as oestrogen, because these compounds have a steroid sulphatase inhibiting action. Moreover, document 1 also indicates that aforementioned compounds act synergistically with anti-oestrogens and aromatase inhibitors; and documents 3 and 4 indicate that aforementioned compounds have an anti-oestrogen action as well as a steroid sulphatase inhibiting action.

In cancer therapy it is conventional practice to use a combination of a plurality of drugs with different mechanisms of action, and use of drugs such as aromatase inhibitors such as vorozole and/or oestrogen receptor antagonists such as ICI 182780 as anti-oestrogens useful for treating oestrogen-dependent cancer is known, as disclosed in document 6. Therefore, a person skilled in

the art could easily conceive of investigating the use of combinations of steroid sulphatase inhibitors disclosed in documents 1-5 with different types of known drugs, beginning with anti-oestrogens, for treating hormone-dependent cancers. Moreover, altering substituent groups in the compounds disclosed in documents 1-5 and attempting to confirm a steroid sulphatase inhibiting action as a result are also within the ordinary competence of a person skilled in the art.